REMARKS

Claims 86-93 are allowed and claims 101 and 102 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The cancellation of claim 101 and the amendment to claim 102 to depend from claim 100, and the amendment to claim 100, render the objection to claims 101 and 102 and the rejection of claims 100 and 103-105 under 35 U.S.C. § 103(a), respectively, moot, as discussed below.

The amendment to claim 105 is supported by Table 3 in the present specification, which table is in Serial No. 60/149,821, one of the priority documents for the above-identified application.

The "Related Application" section of the specification is amended to correct a typographical error. The amendment is supported, for example, by the Filing Receipt.

At paragraph 7 of the Office Action, the Examiner requested copies of the claims of copending, commonly assigned applications having serial numbers 10/159,245, 10/172,363, and 10/601,081. In this regard, the Examiner is requested to consider the attachments enclosed herewith. The Examiner is respectfully requested to note that the claims in Serial No. 10/159,245 are directed to treatment of bone related infection and other non-cancerous conditions in or associated with the bone; Serial No. 10/172,363 was expressly abandoned on November 10, 2003; and the claims in Serial No. 10/601,801 were amended on November 10, 2003 to delete reference to ^{166}Ho-DOTMP.

§ 103 Rejection of the Claims

Claims 100 and 103-105 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Simon et al. (U.S. Patent No. 5,762,907). The amendment of claim 100, as suggested by the Examiner, moots this rejection, and withdrawal of this rejection is respectfully requested. However, the Examiner is requested to note that the divalent metal salts are taught to function by complexing free ligand, not by inhibiting the radiolytic degradation of the complexes (which yields the free ligand that is complexed by the M^{+2} ion)

Claim Objections

Claims 101 and 102 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The cancellation of claim 101, without prejudice or disclaimer, and the amendment of claims 102-103 to depend from claim 100, moot this rejection and withdrawal is respectfully requested.

Conclusion

The Examiner is invited to telephone Applicant's attorney ((612) 373-6959) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743

Respectfully submitted,

ALAN R. FRITZBERG ET AL.

By their Representatives,

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Date November 12, 2003 By _____
Janet E. Embretson
Reg. No. 39,665

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 12th day of November, 2003.

Dawn M. Poole _____ Dawn M. Poole

Name Signature

Docket No. 295.054US1
WD # 532616.doc
NeoRx Corporation Ref. No.: NRX 00088 ICP

SKELETAL-TARGETED RADIATION TO TREAT BONE-ASSOCIATED PATHOLOGIES
Applicant: Alan R. Fritzberg et al.
Serial No: 10/601081

Claims 1-10 were canceled on November 10, 2003 in a Supplemental Preliminary Amendment

Prior to filing a second Supplemental Preliminary Amendment on November 7, 2003, claims 1-35, as of November 6, 2003 (Date first Supplemental Preliminary Amendment was Filed), were as follows.

1. A therapeutic method for treating a bone-associated cancer while reducing the incidence of sustained renal dysfunction comprising:

(a) hydrating a human cancer patient;

(b) parenterally administering a dose of 650-825 mCi/m^2 ^{166}Ho-DOTMP to said patient in an aqueous vehicle comprising an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant;

(c) administering a dose of about 140-200 mg/m^2 melphalan to the patient; and

(d) providing the patient with bone marrow transplantation and/or restoration;

wherein the patient is not subjected to total body irradiation in conjunction with the therapeutic method.

2. The method of claim 1 wherein the patient is refractory to treatment, or in relapse after treatment, with chemotherapy and/or total body irradiation.

3. The method of claim 1 wherein the dose is effective to deliver a mean dose of about 15-30 Gy to the bone marrow of said patient.

4. The method of claim 3 wherein about 200 mg/m^2 melphalan is administered in step (c).

5. The method of claim 1, 2 or 3 wherein the cancer is multiple myeloma.

6. The method of claim 1, 2 or 3 wherein the cancer is metastatic breast cancer or metastatic prostate cancer.

7. The method of claim 1, 2 or 3 wherein the cancer is Ewing's sarcoma.

8. The method of claim 1, 2 or 3 wherein the radioprotectant is an ascorbate or gentisic acid.

9. The method of claim 8 wherein the ascorbate is ascorbic acid at a concentration of about 35-75 mg/ml.

10. The method of claim 9 wherein the vehicle is buffered to about pH 7-8.

Claims 11-13 (Cancelled).

14. A therapeutic method for treating a bone-associated cancer in a human patient comprising:

(a) parenterally administering a dose of ^{153}Sm-EDTMP;

(b) administering a dose of about 140-200 mg/m^2 of melphalan to said patients, wherein steps (a) and/or (b) are effective to suppress the bone marrow of a human patient; and

(c) providing the patient with bone marrow transplantation and/or restoration; wherein the patient is not subjected to total body irradiation in conjunction with the therapeutic method.

15. The method of claim 14 wherein step (c) is carried out while the bone marrow is suppressed by steps (a) and (b).

16. The method of claim 14 wherein the patient is refractory to treatment or in relapse after treatment with chemotherapy and/or total body irradiation.

17. The method of claim 14 wherein the patient is hydrated prior to, during and/or after step (a).

18. The method of claim 14, 15 or 16, wherein the bone-associated cancer is multiple myeloma.

19. The method of claim 1 or 14 wherein the bone marrow transplantation or restoration comprises bone marrow transplantation, stem cell transplantation and/or administration of a colony stimulating factor.

20. The method of claim 14, 15, 16 or 17 wherein the dose of ^{153}Sm-EDTMP is delivered by intravenous infusion or injection in an aqueous vehicle comprising an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant.

21. The method of claim 20 wherein the radioprotectant is an ascorbate or gentisic acid.

22. The method of claim 21 wherein the ascorbate is ascorbic acid at a concentration of about 35-75 mg/ml.

23. The method of claim 14, 15, 16 or 17 wherein the dose delivers about 30-40 Gy of radiation to the bone marrow of the patient.

24. The method of claim 14, 15, 16 or 17 wherein the dose delivers about 15-30 Gy of radiation to the bone marrow of the patient.

25. The method of claim 14, 15, 16 or 17 wherein about 200 mg/m^2 of melphalan is administered.

26. A therapeutic composition comprising:

(a) an amount of ^{153}Sm-EDTMP effective for suppressing the bone marrow of a human;

(b) an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant; and

(c) an aqueous vehicle.

27. The composition of claim 26 wherein the amount of ^{153}Sm-EDTMP is effective to deliver a dose of at least about 15 Gy of radiation to the bone marrow of a human patient.

28. The composition of claim 26 wherein the amount of ^{153}Sm-EDTMP is effective to deliver a dose of about 30-40 Gy of radiation to the bone marrow of a human patient.

29. The composition of claim 26 wherein the amount of ^{153}Sm-EDTMP is effective to deliver a dose of about 20-30 Gy of radiation to the bone marrow of a human patient.

30. The composition of claim 26 wherein the amount of ^{153}Sm-EDTMP is effective to deliver a dose of about 250-3000 MBq/kg to a human patient.

31. The composition of claim 26 wherein the amount of ^{153}Sm-EDTMP is effective to ablate the bone marrow of a human.

32. The composition of claim 26 wherein the radioprotectant is an ascorbate or gentisic acid.

33. The composition of claim 32 wherein the ascorbate is ascorbic acid at a concentration of about 35-75 mg/ml.

34. The composition of claim 26 wherein the vehicle is buffered to about pH 7-8.

35. The method of claim 6 wherein the cancer is metastatic breast cancer.

HIGH DOSE RADIONUCLIDE COMPLEXES FOR BONE MARROW SUPPRESSION
Applicant: Alan R. Fritzberg et al.
Serial No: 10/159245

Claims 50-56, as of August 21, 2003 (date of Office Action).

1-49 (Cancelled).

50. A method for treating infectious diseases in or near bone wherein said method comprises administering to a mammal in need of such treatment a dosage of a radionuclide complexed with a bone targeting ligand, or a physiologically acceptable salt thereof; wherein from about 250 to about 3000 megabecquerels per kilogram of body weight of the radionuclide is administered.

51. The method of claim 50, wherein said infectious disease is selected from the group consisting of osteochondritis, osteomyelitis, soft tissue infection, tuberculous osteomyelitis, osteochondritic syphilis, mycotic osteomyelitis, and periostic syphilis.

52. A method for treating noncancerous diseases in or near bone wherein said method comprises administering to a mammal in need of such treatment a dosage of a radionuclide complexed with a bone targeting ligand, or a physiologically acceptable salt thereof; wherein from about 250 to about 3000 megabecquerels per kilogram of body weight of the radionuclide is administered, without use of TBI.

53. A method of claim 52, wherein the disease is polycythemia vera, macroglobulinemia (Waldenstrom syndrome), megakaryocytic myelosis, or malignant histiocytosis.

54. The method of any one of claims 50, 51, 52, or 53 wherein the radionuclide is ^{153}Sm, ^{90}Y, ^{159}Gd, ^{186}Re, ^{188}Re or ^{166}Ho.

55. The method of claim 54, wherein the radionuclide is ^{166}Ho.

56. The method of any one of claims 50, 51, 52, or 53 wherein about 2000 to about 3000 megabecquerels per kilogram of body weight of the radionuclide is administered.

57-85 (Cancelled).

Docket No. 295.052US1
WD # 532611.doc

NeoRx Corporation Ref. No.: NRX 00088 HCP

SKELETAL TARGETED RADIATION TO TREAT BONE-ASSOCIATED PATHOLOGIES
Applicant: Paul G. Abrams et al.
Serial No: 10/172363

This application was expressly abandoned on November 10, 2003

Prior to abandonment, claims 1-8, as of June 14, 2002 (application filing date) were as follows:

1. A therapeutic method for treating a bone-associated cancer comprising:
   (a) hydrating a human cancer patient;
   (b) parenterally administering a single dose of ^{166}Ho-DOTMP to said patient in an aqueous vehicle comprising an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant, said dose being effective to deliver about 20-50 Gy to the bone marrow of said patient;
   (c) administering a dose of about 140-200 mg/m^2 melphalan to the patient; and
   (d) providing the patient with an autologous stem cell transplant;
wherein the patient is not subjected to total body irradiation in conjunction with the therapeutic method.

2. The method of claim 1 wherein the cancer is multiple myeloma.

3. The method of claim 1 wherein the cancer is metastatic breast or prostate cancer.

4. The method of claim 1 wherein the cancer is Ewing's sarcoma.

5. The method of claim 1, 2 or 3 wherein the radioprotectant is ascorbic acid or gentisic acid.

6. The method of claim 5 wherein the concentration of ascorbic acid is about 35-75 mg/ml.

7. The method of claim 6 wherein the vehicle is buffered to about pH 7-8.

8. The method of claim 5, 7 or 8 wherein the dose is effective to deliver about 20-40 Gy to the bone marrow of said patient.